35. **Gleason score and lethal prostate cancer**

*Jennifer R. Stark, Sven Perner, Meir J. Stampfer, Jennifer A. Sinnott, Stephen Finn, Anna S. Eisenstein, Tobias Kurth, Massimo Loda, Edward L. Giovannucci, Mark A. Rubin*, Lorel A. Mucci*

*Shared senior authorship*

**Background:** Gleason grading is a strong predictor of survival among men with prostate cancer. However, evidence suggests that the prognosis of Gleason score (GS) 7 cancers varies and that GS distribution has changed over time. We aimed to assess the predictive ability of a standardized review compared to original Gleason scoring of radical prostatectomy (RP) specimens, as well as explore potential differences in Gleason 3+4 and Gleason 4+3 cancers, with prostate cancer mortality as the primary endpoint.

**Patients and Methods:** Three study pathologists from an urban hospital in Boston, Massachusetts, conducted a blinded standardized review of 650 RP specimens to assign a primary and secondary Gleason pattern. Tumor specimens were from prostate cancer cases diagnosed between 1984 and 2004 from the Physicians’ Health Study and Health Professionals Follow-Up Study. Lethal prostate cancer was defined as development of bony metastases or prostate cancer death. Hazard ratios (HR) and 95% confidence intervals (95% CI) were estimated according to GS from the original report and standardized review. We compared the discrimination of standardized and original grading with C-statistics obtained from models of 10-year survival.

**Results:** GS 2-5 decreased by 96% in the standardized review compared to the original report, while GS 9-10 increased by 76%. Compared to standardized GS 3+4 cancers, 4+3 cancers were associated with a three-fold increase in lethal prostate cancer (HR: 2.8; 95% CI: 1.0, 7.9). The discrimination of models that included the standardized Gleason data (C-statistic: 0.85) were significantly improved compared to models that included original GS (C-statistic: 0.81).

**Conclusions:** Ignoring the predominance of Gleason pattern 4 in GS 7 cancers may conceal important prognostic information, and a standardized review of GS can markedly improve prediction of prostate cancer survival.